

10
15
20
25
30

WHAT IS CLAIMED IS:

1. An isolated or recombinant nucleic acid comprising a polynucleotide sequence having at least about 70% identity to SEQ ID NO:1, wherein the sequence is distinct from EST Accession no. AA098865.
2. The isolated or recombinant nucleic acid of claim 1, having at least about 80% identity to SEQ ID NO:1.
3. The isolated or recombinant nucleic acid of claim 1, having at least about 90% identity to SEQ ID NO:1.
4. The isolated or recombinant nucleic acid of claim 1, having at least about 95% identity to SEQ ID NO:1.
5. The isolated or recombinant nucleic acid of claim 1, wherein the sequence is less than about 50 kB.
6. The isolated or recombinant nucleic acid of claim 1, wherein the sequence is less than about 25 kB.
7. The isolated or recombinant nucleic acid of claim 1, wherein the sequence is less than about 10 kB.
8. The isolated or recombinant nucleic acid of claim 1, wherein the sequence is less than about 5 kB.
9. The isolated or recombinant nucleic acid of claim 1, wherein the sequence is less than about 2.5 kB.
10. The isolated or recombinant nucleic acid of claim 1, wherein the sequence is between about 2.5 kB and 1 kB, 1 kB and 0.5 kB, 0.5 kB and 0.25 kB and 0.1 kB and 15 base pairs.
11. The isolated or recombinant nucleic acid of claim 1, wherein the sequence is selected from:
 - (a) SEQ ID NO:1;
 - (b) SEQ ID NO:1, wherein one or more T's are U;
 - (c) nucleic acid sequences complementary to (a) or (b); and
 - (d) subsequences of either a, b or c that are at least 15 base pairs long.
12. The isolated or recombinant nucleic acid of claim 1, wherein the sequence is attached to a substrate.

13. The isolated or recombinant nucleic acid of claim 1, wherein the sequence comprises a plurality of sequences attached to a substrate.
14. The isolated or recombinant nucleic acid of claim 13, wherein the sequences are attached at defined positions of the substrate.
15. An isolated nucleic acid that hybridizes to the sequence set forth as SEQ ID NO:1 under stringent hybridization conditions, wherein the nucleic acid is distinct from Accession no. AA098865.
16. The isolated nucleic acid of claim 15, wherein the sequence has a length of about 12-30, 30-50, 50-100, 100-250, 250-500, 500-1000, 1000-2500, 2500-5000 or 5000-10000 base pairs.
17. An expression cassette, comprising a polynucleotide sequence having at least about 70% identity to SEQ ID NO:1 operably linked to an expression control element.
18. The expression cassette of claim 17, wherein the expression control element comprises a promoter or enhancer.
19. The expression cassette of claim 17, wherein the expression control element is constitutive, inducible, tissue-specific or developmentally regulated.
20. The expression cassette of claim 17 further comprising a vector.
21. The expression cassette of claim 20, wherein the vector confers expression in bacteria, plant, insect, mammalian or yeast cell.
22. The expression cassette of claim 20, wherein the vector comprises a viral vector.
23. The expression cassette of claim 22, wherein the viral vector is an adenovirus, retrovirus, adenovirus, adeno-associated virus, lentivirus, reovirus, rotavirus, herpes simplex virus, parvovirus, papilloma virus or cytomegalovirus.
24. The expression cassette of claim 17, wherein the polynucleotide sequence encodes a polypeptide that inhibits apoptosis or an antisense that stimulates or induces apoptosis.
25. The expression cassette of claim 24, wherein the polypeptide comprises SEQ ID NO:2.
26. A transformed cell comprising a nucleic acid of claim 1.

2020/02/05 14:47:00

5

27. The transformed cell of claim 26, where the cell is a bacteria, plant, insect, mammalian or yeast cell.
28. The transformed cell of claim 26, where the mammalian cell is human.
29. A non-human transgenic animal comprising a polynucleotide sequence having at least about 70% identity to SEQ ID NO:1.
30. The non-human transgenic animal of claim 29, wherein the animal expresses a polypeptide or an antisense that modulates apoptosis.
31. The non-human transgenic animal of claim 30, wherein expression of the polypeptide or antisense is tissue-specific.
32. The non-human transgenic animal of claim 30, wherein expression of the polypeptide or antisense is in one or more cells of the heart, brain, lung, kidney, liver, pancreas, spleen, thymus, colon, muscle, leukocyte, small intestine, testis, prostate or ovary.
33. A transgenic plant comprising a nucleic acid sequence having at least about 70% identity to SEQ ID NO:1.
34. The transgenic plant of claim 33, wherein the nucleic acid encodes a polypeptide that modulates apoptosis.
35. The transgenic plant of claim 33, wherein the plant is resistant to abiotic or biotic insult.

20

36. The transgenic plant of claim 35, wherein the biotic insult is induced by a plant pathogen.
37. The transgenic plant of claim 36, wherein the plant pathogen is a virus, a fungus, a bacteria or a nematode.
38. The transgenic plant of claim 35, wherein the abiotic insult is induced by high moisture, low moisture, salinity, nutrient deficiency, air pollution, high temperature, low temperature, soil toxicity, herbicides or insecticides.

25

39. The transgenic plant of claim 33, wherein at least a portion of the plant exhibits a decreased level of senescence.
40. A seed capable of germinating into a plant having in its genome a heterologous nucleic acid sequence having at least about 70% identity to SEQ ID NO:1.

5

41. The seed of claim 40, wherein the nucleic acid encodes a polypeptide that modulates apoptosis in a germinated plant cell.
42. An isolated or recombinant nucleic acid having at least about 70% identity to SEQ ID NO:1, wherein the nucleic acid encodes a polypeptide that modulates apoptosis.
43. The isolated nucleic acid of claim 42, wherein the nucleic acid has at least about 80% identity to SEQ ID NO:1.
44. The isolated nucleic acid of claim 42, wherein the nucleic acid has at least about 90% identity to SEQ ID NO:1.
45. The isolated nucleic acid of claim 42, wherein the nucleic acid has at least about 95% identity to SEQ ID NO:1.
46. An isolated or recombinant polypeptide comprising a sequence having at least about 65% identity to SEQ ID NO:2, and having one or more activities of the polypeptide set forth in SEQ ID NO:2.
47. The isolated or recombinant polypeptide of claim 46 having at least about 75% identity to SEQ ID NO:2.
48. The isolated or recombinant polypeptide of claim 46 having at least about 85% identity to SEQ ID NO:2.
49. The isolated or recombinant polypeptide of claim 46 having at least about 90% identity to SEQ ID NO:2.
50. The isolated or recombinant polypeptide of claim 46 having at least about 95% identity to SEQ ID NO:2.
51. The isolated or recombinant polypeptide of claim 46, wherein the polypeptide is at least about 50, 75, 125, 150 or 200 amino acids in length.

20

52. The isolated or recombinant polypeptide of claim 46, wherein the polypeptide contains a transmembrane domain substantially the same as the underlined amino acid sequence set forth in Figure 1A (SEQ ID NO:13).
53. The isolated or recombinant polypeptide of claim 46, wherein the transmembrane domain comprises the underlined amino acid sequence set forth in Figure 1A (SEQ ID NO:13).

25

30

5 54. The isolated or recombinant polypeptide of claim 46, wherein the transmembrane domain comprises a mitochondrial protein or a Bcl-2 protein family member transmembrane domain.

10 55. The isolated or recombinant polypeptide of claim 46, wherein the activity is selected from modulating apoptosis, homodimerization, heteromerization, binding to Bcl-2, Bcl-XL or Bax, forming a membrane channel, associating with mitochondria, or immunogenicity.

15 56. The isolated or recombinant polypeptide of claim 46, wherein the polypeptide modulates apoptosis in bacteria, plant, insect, mammalian or yeast cell.

20 57. The isolated or recombinant polypeptide of claim 56, wherein the human cell is a heart, brain, lung, kidney, liver, pancreas, spleen, thymus, colon, leukocyte, small intestine, testis, prostate or ovarian cell.

25 58. The isolated or recombinant polypeptide of claim 46, wherein the polypeptide inhibits Bax mediated apoptosis.

60 59. The isolated or recombinant polypeptide of claim 46, wherein the polypeptide does not detectably inhibit Bak mediated apoptosis.

65 60. The isolated or recombinant polypeptide of claim 46, wherein the polypeptide contains one or more BH1, BH2, BH3 or BH4 domains set forth in Figure 1A.

70 61. The isolated or recombinant polypeptide of claim 46, wherein the polypeptide is attached to a substrate.

75 62. The isolated or recombinant polypeptide of claim 46, wherein the polypeptide comprises a plurality of polypeptides attached to a substrate.

80 63. The isolated or recombinant polypeptide of claim 62, wherein the polypeptides are attached at defined positions of the substrate.

85 64. An antibody that specifically binds to a polypeptide comprising a sequence set forth in SEQ ID NO:2, or an immunogenic subsequence thereof.

90 65. The antibody of claim 64, wherein the antibody modulates an activity of Bcl-B.

95 66. The antibody of claim 64, wherein the activity comprises modulating apoptosis.

100 67. The antibody of claim 64, wherein the antibody is attached to a substrate.

105 68. The antibody of claim 64, wherein the antibody comprises a plurality of antibodies attached to a substrate.

5 69. The antibody of claim 68, wherein the antibodies are attached at defined positions of the substrate.

70. A chimeric polypeptide comprising a sequence having at least about 65% identity to SEQ ID NO:2 and a second polypeptide sequence.

71. The chimeric polypeptide of claim 70, wherein the second polypeptide sequence comprises a tag.

72. The chimeric polypeptide of claim 70, wherein the portion of the chimera having at least about 65% identity to SEQ ID NO:2 is encoded by a polynucleotide sequence having at least about 70% identity to SEQ ID NO:1.

73. A kit comprising a nucleic acid of claim 1, a polypeptide of claim 46, or an antibody of claim 64 in a container.

74. The kit of claim 73, wherein the container includes instructions for detecting a polynucleotide sequence having at least about 70% identity to SEQ ID NO:1, a polynucleotide or polypeptide that binds to a polypeptide of claim 46, or a polypeptide comprising a sequence set forth in SEQ ID NO:2.

75. A composition comprising an isolated or recombinant nucleic acid of claim 1, a polypeptide of claim 46, or an antibody of claim 64 in a pharmaceutically acceptable carrier.

20 76. A method of producing a polypeptide comprising expressing a nucleic acid encoding an amino acid sequence having at least about 65% identity to SEQ ID NO:2.

77. The method of claim 76, wherein the nucleic acid is expressed in solution, or in a cell *in vitro* or *in vivo*.

25 78. A method for detecting the presence of a polynucleotide sequence encoding an amino acid sequence having at least about 65% identity to SEQ ID NO:2, or a polypeptide of claim 46, comprising:

30 (a) contacting a sample with a polynucleotide sequence having at least about 70% identity to SEQ ID NO:1 or an antibody of claim 64, respectively;

(b) and detecting the presence of a polynucleotide sequence encoding an amino acid sequence having at least about 65% identity to SEQ ID NO:2, or a polypeptide of claim 46 in the sample.

10 5 15 20 25 30

79. A method for modulating apoptosis of a cell comprising contacting the cell with the polypeptide of claim 46, a nucleic acid of claim 42, or an antibody of claim 65 in an amount sufficient to modulate apoptosis in the cell.

80. The method of claim 79, wherein apoptosis is induced or increased.

81. The method of claim 79, wherein apoptosis is prevented or inhibited.

82. The method of claim 79, wherein the cell is at risk of apoptosis or is undergoing apoptosis.

83. The method of claim 79, wherein the cell expresses Bax.

84. The method of claim 79, wherein the cell is selected from heart, brain, lung, kidney, liver, pancreas, spleen, thymus, colon, leukocyte, small intestine, testis, prostate or ovarian cells.

85. The method of claim 79, wherein the cell is present in a subject.

86. The method of claim 85, wherein the subject is at risk of or is suffering from a disorder associated with apoptosis.

87. The method of claim 86, wherein the disorder comprises a cell degenerative or proliferative disorder.

88. The method of claim 87, wherein the degenerative disorder comprises neural or muscle degeneration.

89. The method of claim 86, wherein the disorder is selected from Alzheimer's disease, Parkinson's disease, Creutzfeldt-Jacob's disease (CJD), Huntington disease (HD), Machado-Joseph disease (MJD), Spinocerebellar ataxias 1, 2 and 6 (SCA-1, -2 and -6), dentatorubropallidolysian atrophy (DRPLA), Kennedy's disease, ischemia, stroke and head trauma.

90. A method for treating a subject having or at risk of a disorder associated with apoptosis, comprising administering to the subject an amount of the polypeptide of claim 46, the nucleic acid of claim 42 or an antisense thereof, or an antibody of claim 65 sufficient to treat the subject having or at risk of the disorder associated with apoptosis.

91. The method of claim 90, wherein the disorder comprises a cell degenerative or proliferative disorder.

5 92. The method of claim 91, wherein the degenerative disorder comprises neural or muscle degeneration.

93. The method of claim 90, wherein the disorder is selected from Alzheimer's disease, Parkinson's disease, Creutzfeldt-Jacob's disease (CJD), Huntington disease (HD), Machado-Joseph disease (MJD), Spinocerebellar ataxias 1, 2 and 6 (SCA-1, -2 and -6), dentatorubropallidoluysian atrophy (DRPLA), Kennedy's disease, ischemia, stroke and head trauma.

94. The method of claim 90, wherein the antisense comprises a sequence complementary to Bcl-B sense strand, a sequence that forms a triplex with Bcl-B, a ribozyme, a DNAzyme or an RNAi molecule.

95. A method for modulating apoptosis of a cell, comprising contacting the cell with an antisense sequence having at least about 70% identity to SEQ ID NO:1, a dominant negative Bcl polypeptide or an antibody of claim 65 in an amount sufficient to modulate apoptosis in the cell.

96. The method of claim 95, wherein apoptosis is induced or increased.

97. The method of claim 95, wherein apoptosis is prevented or inhibited.

98. The method of claim 95, wherein the antisense sequence comprises a sequence complementary to Bcl-B sense strand, a sequence that forms a triplex with Bcl-B, a ribozyme, a DNAzyme or an RNAi molecule.

20 99. The method of claim 95, wherein antisense expression is conferred by an expression control element.

100. The method of claim 95, wherein the cell is selected from heart, brain, lung, kidney, liver, pancreas, spleen, thymus, colon, muscle, leukocyte, small intestine, testis, prostate or ovarian cells.

25 101. The method of claim 95, wherein the cell is at risk of undesirable proliferation or is hyperproliferating.

102. The method of claim 95, wherein the cell is present in a subject.

103. The method of claim 102, wherein the subject is at risk of or is suffering from a cell degenerative or proliferative disorder.

30 104. The method of claim 103, wherein the cell proliferative disorder comprises a neoplasia, autoimmune disorder or fibrotic condition.

5

10

15

20

25

30

105. A method for identifying a gene or agent that modulates expression of a polypeptide having at least about 65% identity to SEQ ID NO:2 comprising:
 - (a) contacting a cell that expresses the polypeptide with a test gene or test agent; and
 - (b) measuring expression of the polypeptide or nucleic acid encoding the polypeptide, wherein an increase or decrease in the amount of the polypeptide or nucleic acid encoding the polypeptide identifies the test gene or test agent as a modulator of the polypeptide's expression.
106. The method of claim 105, wherein the cell is a bacteria, plant, insect, mammalian or yeast cell.
107. The method of claim 105, wherein the cell has been transformed with a nucleic acid that encodes the polypeptide.
108. The method of claim 105, wherein the test gene or test agent comprises a library of genes or agents.
109. A method for identifying a gene or agent that modulates activity of a polypeptide having at least 65% identity to SEQ ID NO:2 comprising:
 - (a) contacting a cell that expresses the polypeptide with a test gene or test agent; and
 - (b) measuring activity of the polypeptide or nucleic acid encoding the polypeptide, wherein an increase or decrease in the activity of the polypeptide or nucleic acid encoding the polypeptide identifies the test gene or test agent as a modulator of the polypeptide's activity.
110. The method of claim 109, wherein the activity comprises increased or decreased cellular apoptosis, DNA fragmentation or caspase activity.
111. The method of claim 109, wherein the cell is a bacteria, plant, insect, mammalian or yeast cell.
112. The method of claim 111, wherein the yeast cell expresses Bax and the activity modulated comprises increased or decreased Bax-mediated yeast cell death.
113. The method of claim 111, wherein the yeast are SOD-deficient and the activity modulated comprises increased or decreased Bcl-B mediated yeast cell survival.

5 114. The method of claim 109, wherein the cell has been transformed with a nucleic acid that encodes the polypeptide.

10 115. The method of claim 109, wherein the test gene or test agent comprises a library of genes or agents.

15 116. A method for identifying an agent that modulates activity of a polypeptide having at least about 65% identity to SEQ ID NO:2 comprising:
(a) contacting a membrane channel created with the polypeptide under conditions allowing transport of a molecule through the membrane channel with a test agent; and
(b) measuring transport of the molecule in the presence of the agent in comparison to transport in the absence of the agent, wherein increased or decreased transport of the molecule in the presence of the test agent identifies an agent that modulates activity of a polypeptide having at least about 65% identity to SEQ ID NO:2.

20 117. The method of claim 116, wherein the polypeptide comprises a BH4 domain.

118. The method of claim 116, wherein the membrane is synthetic or natural.

119. The method of claim 116, wherein the molecule comprises an ion.

25 120. A method for identifying a molecule that binds to a polypeptide having at least about 65% identity to SEQ ID NO:2 comprising contacting the polypeptide with a test molecule and determining whether the test molecule binds to the polypeptide.

121. The method of claim 120, wherein the polypeptide contains one or more 15N-labeled amino acids, and the binding is detected by resonance changes in the polypeptide.

122. The method of claim 120, wherein the test molecule comprises a polypeptide sequence.

25 123. The method of claim 120, wherein the polypeptide sequence comprises an antibody.

124. The method of claim 120, wherein the test molecule is attached to the surface of a substrate, or the polypeptide is attached to the surface of a substrate.

30 125. The method of claim 120, wherein the test molecule comprises a library of molecules.

126. The method of claim 125, wherein the library is attached at discrete positions of a substrate.

127. The method of claim 120, wherein the contacting is in solution, in solid phase, in a cell or in situ.

5 128. A method for detecting Bcl-B in a sample comprising:
(a) contacting a sample having or suspected of having Bcl-B protein or nucleic acid encoding Bcl-B with an antibody of claim 64 or nucleic acid having at least about 70% identity to SEQ ID NO:1 under conditions allowing binding;
(b) separating bound protein or nucleic acid from unbound protein or nucleic acid; and
(c) determining the amount of Bcl-B protein or nucleic acid having about 70% identity to SEQ ID NO:1 thereby detecting Bcl-B in the sample.

129. The method of claim 128, wherein the contacting is in solution, in solid phase, in a cell or in situ.

130. The method of claim 128, wherein the sample was obtained from a subject having or at risk of having a cell proliferative or degenerative disorder.

131. The method of claim 130, wherein the cell proliferative disorder comprises hyperproliferation.

20 132. The method of claim 130, wherein the cell proliferative disorder comprises undesirable apoptosis.

133. A method of identifying an agent that modulates binding of a polypeptide having at least about 65% identity to SEQ ID NO:2 to a molecule comprising:
(a) contacting the polypeptide with a binding molecule under conditions allowing binding, in the presence and absence of a test agent; and
(b) measuring binding between the polypeptide and the molecule in the presence and absence of the test agent, wherein increased or decreased binding identifies an agent that modulates binding of a polypeptide having at least about 65% identity to SEQ ID NO:2.

25 134. The method of claim 133, wherein the binding molecule comprises a Bcl-B protein.

5

135. The method of claim 133, wherein the binding molecule comprises a Bcl-2 protein family member.

136. The method of claim 135, wherein the Bcl-2 protein family member comprises Bcl-2, Bcl-XL or Bax.

137. The method of claim 133, wherein the polypeptide comprises a Bcl-B domain.

138. The method of claim 133, wherein the contacting is in solution, in solid phase or in a cell.

139. The method of claim 138, wherein the cell is a bacteria, plant, insect, mammalian or yeast cell.

140. The method of claim 139, wherein the assay comprises a two-hybrid system for expressing the polypeptide and the binding molecule.

141. The method of claim 133, wherein the binding is measured by detecting fluorescence of the polypeptide conjugated to a fluorophore.